Expanded Criteria Donors

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KEYWORDS

• Deceased donor • Surgery • Outcomes • Steatosis • Donor age

KEY POINTS

- The expanded criteria donor graft connotes an organ with characteristics associated with suboptimal transplant outcomes that fall into 2 categories of risk: (1) graft dysfunction and (2) disease transmission.
- Graft characteristics associated with increased risk of graft dysfunction include older donor age, donation after cardiac death, large droplet steatosis, prolonged cold ischemia time.
- Donor characteristics associated with increased risk of disease transmission include positive hepatitis B core antibody, positive hepatitis C antibody, behaviors known to be associated with increased risk of human immunodeficiency virus, hepatitis B or C infection, and known history of malignancy.

THE SPECTRUM OF DONOR QUALITY: IDEAL, STANDARD, AND EXPANDED

The ideal deceased donor liver, a whole liver from a brain dead donor less than 40 years of age who died of trauma, is well defined. The standard graft and the expanded liver graft are, in contrast, relative concepts that may evolve with time. A standard liver connotes an organ of average quality relative to the spectrum currently utilized for transplantation, while an expanded liver connotes an organ of lower than average quality, coming from a donor with characteristics known to be associated with suboptimal transplant outcomes. There is general consensus that the criteria fall into 2 categories of risk: (1) graft dysfunction and (2) disease transmission.

Donor Risk Factors for Graft Dysfunction

Older donor age

Although the young adult donor is widely recognized as ideal, utilization of livers from older donors represents a logical means to expand the donor pool. In the nontransplant setting, the liver's physiologic function remains well preserved throughout life, likely a result of its unique regenerative capacity.[1] However, in the transplant setting,

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liver grafts from older donors are associated with a higher risk of graft failure and mortality.[2–11] Although there is marked heterogeneity in the age cut-offs used to define an older donor, decreased patient and graft survival rates have been reported regardless of the age cut-off used: 50, 60, or 70 years.[4–7] From 2008 to 2012, 1-year unadjusted graft survival for recipients of grafts from donors younger than 40 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years and older was 88%, 86%, 84%, 85%, and 82%, respectively ($P<.001$).[12]

There are at least 2 probable mechanisms for this age-related increased risk of liver allograft failure. First, older hepatic parenchyma has increased vulnerability to ischemia/reperfusion injury owing to relatively fewer hepatocytes and decreased regenerative capacity.[1] In mouse models, older livers demonstrate significantly more necrosis and neutrophil accumulation[13] and lower hepatic expression of heat shock proteins that protect hepatocytes from cellular injury.[14] A second, and potentially synergistic, mechanism is the increased burden of medical comorbidities in older donors. Obesity, diabetes, hypertension, and dyslipidemia may lead to hepatic steatosis and atherosclerotic disease,[8,15,16] further increasing susceptibility to injury.

The vulnerability of livers from older deceased donors manifests in multiple pathways of allograft dysfunction or failure. Several studies have shown that older donor livers are associated with primary nonfunction (PNF), defined as initial poor function requiring retransplantation or causing death within 7 days of transplantation.[11,17–19] Recipients of older livers have increased rates of hepatic artery thrombosis[16,20,21] and more severe ischemia reperfusion injury.[9,13,14] Higher rates of biliary complications and cholestasis have also been reported among recipients of livers from donors at least 60 years of age.[5,7] Finally, longer transplant hospitalization length of stay, higher transplant costs, and increased resource utilization are strongly associated with livers with a higher donor risk index, a metric of donor quality dominated by donor age.[22–24]

Interestingly, donor age exerts a differential impact on recipients with chronic hepatitis C virus (HCV) infection. Studies have consistently shown an interaction between older donor age and positive recipient HCV status that predisposes to fibrosing cholestatic hepatitis, more rapid fibrosis, post-transplant infections, graft failure, and mortality.[10,19,25–34] Although age cut-offs defining an older donor for HCV recipients has varied, the negative impact appears to begin at 40 years of age. In an analysis of data on all adult primary, single-organ liver transplants from 1995 to 2001, there was a statistically significant increase in graft loss for every decade increase in donor age starting at 40 years among HCV-infected recipients but not until 60 years in non-HCV-infected recipients (**Fig. 1**).[10]

Utilization of livers from deceased donors of advanced age continues to rise throughout the world,[35–38] and there is currently no consensus on an upper age limit for liver donors. One strategy to minimize risk is to have a lower biopsy threshold. A second strategy is to minimize cold ischemia time (CIT).[6,16,39] This can be accomplished through careful recipient selection, avoiding candidates expected to require protracted dissection, and through careful coordination between organ procurement and initiation of recipient surgery. In 1 Italian study of 178 patients who received livers from donors at least 60 years of age, grafts transplanted with less than 7 versus 7 or more hours of CIT demonstrated significantly higher graft survival at 1 year (84% vs 71%) and 3 years (76% vs 54%) [$P<.005$].[39] Lastly, experts have generally agreed that HCV-infected recipients are suboptimal candidates for older donor livers. This belief is likely to evolve with the availability of increasingly effective and tolerable direct-acting antiviral agents against HCV.